JAMA Internal Medicine | Review

Management of Orthostatic Hypotension
A Review

David Moloney, MD; Ayman Youssef, MD, PhD; Luis E. Okamoto, MD

IMPORTANCE Orthostatic hypotension is a common but underrecognized condition that increases with age and is associated with a lower quality of life, falls, and increased mortality. The frequent coexistence of supine hypertension and postprandial hypotension with orthostatic hypotension makes it a challenging condition to manage.

OBSERVATIONS Testing for orthostatic hypotension should be done in patients with orthostatic symptoms (eg, vision changes and dizziness that occur only when upright and improve when seated or lying down), as well as asymptomatic patients in high-risk groups such as adults with frailty who are older than 70 years, individuals with neurodegenerative or autonomic disorders, and patients with unexplained falls. Patients with orthostatic hypotension should be screened for postprandial hypotension and supine hypertension to inform the treatment approach. Nonpharmacological strategies, such as medication review, increased salt and fluid intake, compression garments, and behavioral modifications, serve as fundamental approaches to treat orthostatic hypotension. Midodrine and droxidopa are the only US Food and Drug Administration–approved medications for orthostatic hypotension, but other medications (eg, fludrocortisone, atomoxetine, pyridostigmine) are used off label as part of an individualized treatment plan. Treatment targets in orthostatic hypotension are focused not on blood pressure measurements but on symptom relief and fall prevention.

CONCLUSIONS AND RELEVANCE All patients with orthostatic symptoms—along with other select patient groups—should be evaluated for orthostatic hypotension. Nonpharmacological treatments are first line, and medication decisions should be tailored based on clinical presentation and relevant comorbidities.

JAMA Intern Med. doi:10.1001/jamainternmed.2026.0284
Published online April 6, 2026.

CME at jamacmelookup.com

Author Affiliations: Vanderbilt Autonomic Dysfunction Center, Division of Genetic Medicine and Clinical Pharmacology, Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee.

Corresponding Author: Luis E. Okamoto, MD, Vanderbilt Autonomic Dysfunction Center, Division of Genetic Medicine and Clinical Pharmacology, Department of Medicine, Vanderbilt University Medical Center, 1161 21st Ave S, Suite S3120A MCN, Nashville, TN 37232-2600 (luis.e.okamoto@vumc.org).

Orthostatic hypotension (OH), a condition characterized by the failure to maintain blood pressure (BP) while standing, is commonly encountered in primary care settings.[1,2] It is particularly prevalent (>20%)[1] in patients older than 60 years and among those in long-term care facilities (31% vs 17% in community settings).[3] OH considerably affects quality of life[4] and is associated with increased falls,[5] fractures,[6] and mortality.[7]

OH is difficult to diagnose due to variable presentations. It is often associated with nonspecific symptoms such as lightheadedness, weakness, fatigue, visual blurring, and neck and shoulder pain (known as coat-hanger pain), although these are not necessary for the diagnosis. Some patients with OH are altogether asymptomatic, although even this group experiences a higher risk of unexplained falls.[8]

Because patients with OH often first present in primary care settings; internists must be prepared to recognize potential OH and assess its character, effects on patient health, and underlying cause. While certain medications and diagnostic tests typically fall under the purview of autonomic specialists, a large portion of the recommended evaluation and initial approach to treatment can be undertaken in primary care. This review aims to present important diagnostic and treatment approaches for a generalist audience to improve confidence in managing this important medical condition.

Methods

We conducted a search on PubMed for systematic reviews and meta-analyses, Cochrane reviews, and professional society and government guidelines published between 1980 and March 2025. We then undertook a manual review of the bibliographies. The search strategy combined *orthostatic hypotension* with the following terms: *treatment*, *lifestyle*, *non-pharmacological*, *drugs*, *medication*, *pharmacotherapy*, and *therapy*.

Discussion

Pathophysiology

On standing, there is normally a gravity-induced blood pooling of 0.7 to 1 L in the lower body, mainly in splanchnic vessels, resulting in decreased venous return and a transient drop in cardiac output and BP.

© 2026 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.
Downloaded from jamanetwork.com by guest on 04/07/2026

SHOUT
SHARE
IT

Box. Conditions That Can Cause or Exacerbate Orthostatic Hypotension

- Nonneurogenic orthostatic hypotension
  - Medications (eg, vasodilators, β-blockers, central α-2 agonists, diuretics)
  - Hypovolemia (eg, dehydration, hemorrhage/anemia, diarrhea/vomiting)
  - Excessive venous pooling (eg, venous stasis of lower limbs, deconditioning, hot environment, prolonged standing)
  - Cardiac disorders (eg, arrhythmias, heart failure with reduced ejection fraction, aortic stenosis, myocarditis)
- Neurogenic orthostatic hypotension
  - Primary autonomic failure: pure autonomic failure, Parkinson disease, multiple system atrophy, and dementia with Lewy bodies
  - Secondary forms of autonomic failure (systemic conditions)
    - Peripheral autonomic neuropathy (eg, diabetes, amyloidosis, B_{12} deficiency, toxic and metabolic neuropathies)
    - Autoimmune autonomic disorders (eg, autoimmune autonomic ganglionopathy, paraneoplastic syndrome, Sjogren syndrome)
    - Spinal cord disorders (eg, tetraplegia)

Carotid and aortic baroreceptors sense this BP drop and trigger compensatory sympathetic activation and parasympathetic withdrawal, increasing peripheral resistance and heart rate, and decreasing venous capacitance.[9] In patients with OH, this compensatory mechanism does not function properly, leading to orthostatic symptoms.

Classical OH is defined as a sustained reduction in systolic BP of 20 mm Hg or greater (≥30 mm Hg in patients with supine hypertension) or diastolic BP of 10 mm Hg or greater within 3 minutes of standing or head-up tilt at 60°.[10] However, milder or transient reductions in upright BP can also cause clinically meaningful orthostatic symptoms. Delayed OH, defined as a progressive BP fall after 3 minutes of standing or head-up tilt,[11] is a milder form of OH that occurs in patients with neurodegenerative autonomic diseases or incomplete autonomic dysfunction,[2,12] with half progressing to classical OH within 10 years.[13]

Two main categories of conditions contribute to OH. First, neurogenic OH (nOH) is caused by autonomic disorders that arise from either primary neurodegenerative diseases such as Parkinson disease, multiple system atrophy, Lewy body dementia, and pure autonomic failure, or systemic conditions that affect peripheral nerves, including autoimmune autonomic disorders, autonomic peripheral neuropathies (eg, diabetes-related peripheral neuropathies), and spinal cord disorders (**Box**). nOH due to diabetes neuropathy, neurodegenerative diseases, and amyloidosis are the most frequent causes of chronic OH.

The second category is non–neurogenic OH (non-nOH), which is caused by cardiac disease or reversible factors (eg, hypovolemia, medications) that impair neural or hemodynamic compensatory responses to standing (Box). Non-nOH often has an acute or subacute presentation and can occur in patients with underlying autonomic dysfunction, in whom these aggravating factors overwhelm the patient's reduced autonomic reserve.[14-16]

Assessment and Diagnosis of OH

All patients presenting with orthostatic symptoms (ie, symptoms that occur only when upright and improve when seated or lying down) should be assessed for OH.[11] Screening for OH is recommended in those with neurodegenerative diseases (eg, Parkinson disease), peripheral autonomic neuropathies, unexplained falls, or syncope,[11,17] and patients older than 70 years who have frailty or are receiving polypharmacy treatment.[11]

Initial diagnostic testing for OH is typically performed in clinic with an active stand test (AST). In this test, BP and heart rate are measured after lying down for 5 minutes or longer, then immediately on standing and every minute for up to 3 minutes. Orthostatic symptoms such as positional dizziness are also assessed during the test. The AST is most sensitive if performed in the morning, when OH symptoms are typically more prominent.[18,19] The clinician can suspect nOH if the ratio of change in heart rate and change in systolic BP (defined as the change in heart rate from supine divided by the fall in systolic BP at 3 minutes of standing) is lower than 0.5 (91% sensitivity and 88% specificity).[20] If a high suspicion for OH remains after an initial negative test, it can be repeated in clinic or at home. Home-based AST has been shown to be feasible and reliable in older adults[21-23] and may allow repeat orthostatic measurements based on time of day, symptoms, or potential triggers, thereby improving its sensitivity and reproducibility.[18,21,24] The AST can also be extended to 10 minutes to better detect delayed OH. Patients can be referred to a specialist center, if available, to facilitate these tests, along with more advanced testing, such as beat-to-beat BP monitoring to assess for transient forms of OH or head-up tilt testing.

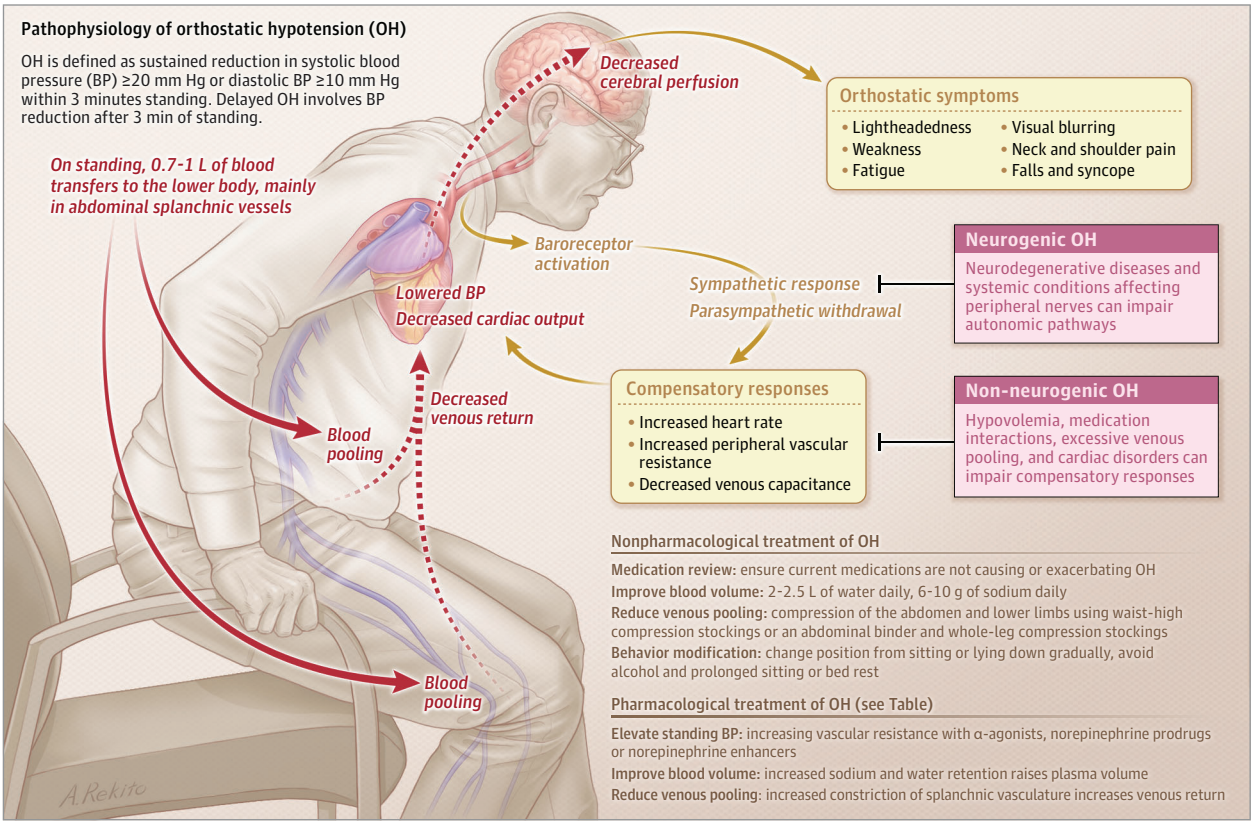
The sit-to-stand test and the head-up tilt tests are alternatives to the AST. The sit-to-stand test is an alternative when the AST cannot be performed, as it does not require an examination table. In this test, BP and heart rate are measured after sitting for 5 minutes or longer, then at 1 and 3 minutes of standing. The diagnostic sensitivity of this test, however, is much lower than that of the AST.[25-30] Lower cutoff values (eg, >15/7 mm Hg) have been proposed to improve sensitivity, but they still need validation.[25] Similar to the AST, the sit-to-stand test can be performed either in the office or at home. The head-up tilt test is time consuming and requires trained personnel and specialized equipment, but it offers the most comprehensive assessment, including beat-to-beat BP, electrocardiogram, and electroencephalogram.

Once the diagnosis of OH is confirmed, a detailed medical history and physical examination are essential to characterize the condition (ie, nOH vs non-nOH), identify a cause, guide additional diagnostic testing, and inform treatment (**Figure 1**). The history should include a thorough medication review, looking for medications that can cause or worsen OH (Box). It should also ask about potential aggravating factors, such as rapid postural changes, prolonged standing, exposure to hot environments, and deconditioning. Since falls among older people are often multifactorial, the history should include a multidomain falls risk assessment inquiring about the frequency, context, and consequences of previous falls; mobility and neurological symptoms (eg, problems with gait, balance, muscle strength, vision, and vestibular or cognitive function); and syncope to inform individualized tailored interventions that, in addition to OH treatment, help prevent or reduce falls and injuries.[17]

Certain features of the medical history may serve as important clues for more rare causes of OH. For example, paraneoplastic and autoimmune ganglionopathies should be considered in patients with nOH of subacute onset or with an underlying cancer. Patients with a history of head and neck surgery or radiotherapy may experience

© 2026 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.
Downloaded from jamanetwork.com by guest on 04/07/2026

Figure 1. Pathophysiology of Orthostatic Hypotension


Pathophysiology of orthostatic hypotension (OH)
OH is defined as sustained reduction in systolic blood pressure (BP) ≥20 mm Hg or diastolic BP ≥10 mm Hg within 3 minutes standing. Delayed OH involves BP reduction after 3 min of standing.
On standing, 0.7-1 L of blood transfers to the lower body, mainly in abdominal splanchnic vessels
Decreased cerebral perfusion
Orthostatic symptoms
Lightheadedness
Weakness
Fatigue
Visual blurring
Neck and shoulder pain
Falls and syncope
Baroreceptor activation
Lowered BP
Decreased cardiac output
Sympathetic response
Parasympathetic withdrawal
Neurogenic OH
Neurodegenerative diseases and systemic conditions affecting peripheral nerves can impair autonomic pathways
Decreased venous return
Blood pooling
Compensatory responses
Increased heart rate
Increased peripheral vascular resistance
Decreased venous capacitance
Non-neurogenic OH
Hypovolemia, medication interactions, excessive venous pooling, and cardiac disorders can impair compensatory responses
Blood pooling
A Rekito
Nonpharmacological treatment of OH
Medication review: ensure current medications are not causing or exacerbating OH
Improve blood volume: 2-2.5 L of water daily, 6-10 g of sodium daily
Reduce venous pooling: compression of the abdomen and lower limbs using waist-high compression stockings or an abdominal binder and whole-leg compression stockings
Behavior modification: change position from sitting or lying down gradually, avoid alcohol and prolonged sitting or bed rest
Pharmacological treatment of OH (see Table)
Elevate standing BP: increasing vascular resistance with α-agonists, norepinephrine prodrugs or norepinephrine enhancers
Improve blood volume: increased sodium and water retention raises plasma volume
Reduce venous pooling: increased constriction of splanchnic vasculature increases venous return

afferent baroreflex failure, which presents with highly labile systolic BP ranging from 80 to 180 mm Hg in a 24-hour period.[31] Autonomic neuropathy secondary to light chain or transthyretin amyloidosis should be considered in patients with OH, weight loss, and gastrointestinal symptoms. Finally, OH can be the initial presenting symptom of adrenal insufficiency. Specialized testing at a tertiary center may be required for some conditions, such as cardiac and autonomic disorders, or when postural symptoms are suspected to be unrelated to OH (eg, neurologic, vestibular, psychiatric disorders).

The physical examination may be useful for identifying the underlying cause in select settings, including dehydration or hypovolemia, neurological conditions associated with OH (eg, parkinsonism, peripheral neuropathy), and cardiac disorders (eg, arrhythmias, valvular disorders, heart failure). Initial testing should include a complete blood cell count to assess for anemia or infection, a basic metabolic panel to look for diabetes or electrolyte imbalance associated with volume depletion, and an electrocardiogram to evaluate for arrhythmias. Additional testing (eg, vitamin B_{12}, cortisol) should be guided by the clinical history and physical examination.

Supine Hypertension and Postprandial Hypotension

It is also important to assess for supine hypertension and postprandial hypotension, 2 conditions frequently associated with nOH. Supine hypertension, defined as a supine systolic BP of 140 mm Hg or higher and/or diastolic BP of 90 mm Hg or higher, occurs in 50% or more of patients with autonomic failure.[32] Supine hypertension is associated not only with hypertensive end-organ damage in the long term, but also with nighttime pressure diuresis, which worsens OH in the morning.

Postprandial hypotension is caused by the inability to compensate for the splanchnic blood pooling after eating. It is defined as a drop in systolic BP of more than 20 mm Hg within 2 hours of eating, especially carbohydrate-rich meals.[33] If left untreated, it can worsen OH and increase the risk of syncope and falls.

Twenty-four–hour ambulatory BP monitoring can be useful for detecting postprandial hypotension and nighttime supine hypertension.[11,34,35] However, BP measurements should be accompanied by a detailed diary noting body posture, mealtimes, medications, and sleep to determine whether meals or nighttime sleep are associated with low or high BP, respectively.[35] Alternatively, postprandial hypotension can be assessed at home by measuring BP every 10 minutes for 2 hours after eating in the seated or supine position.[36] Because supine hypertension and postprandial hypotension often occur together, we recommend screening for both conditions if one is identified.[37] Ambulatory monitoring can also be useful to detect hypotension in patients with suspected OH who do not meet OH criteria in clinic.[35]

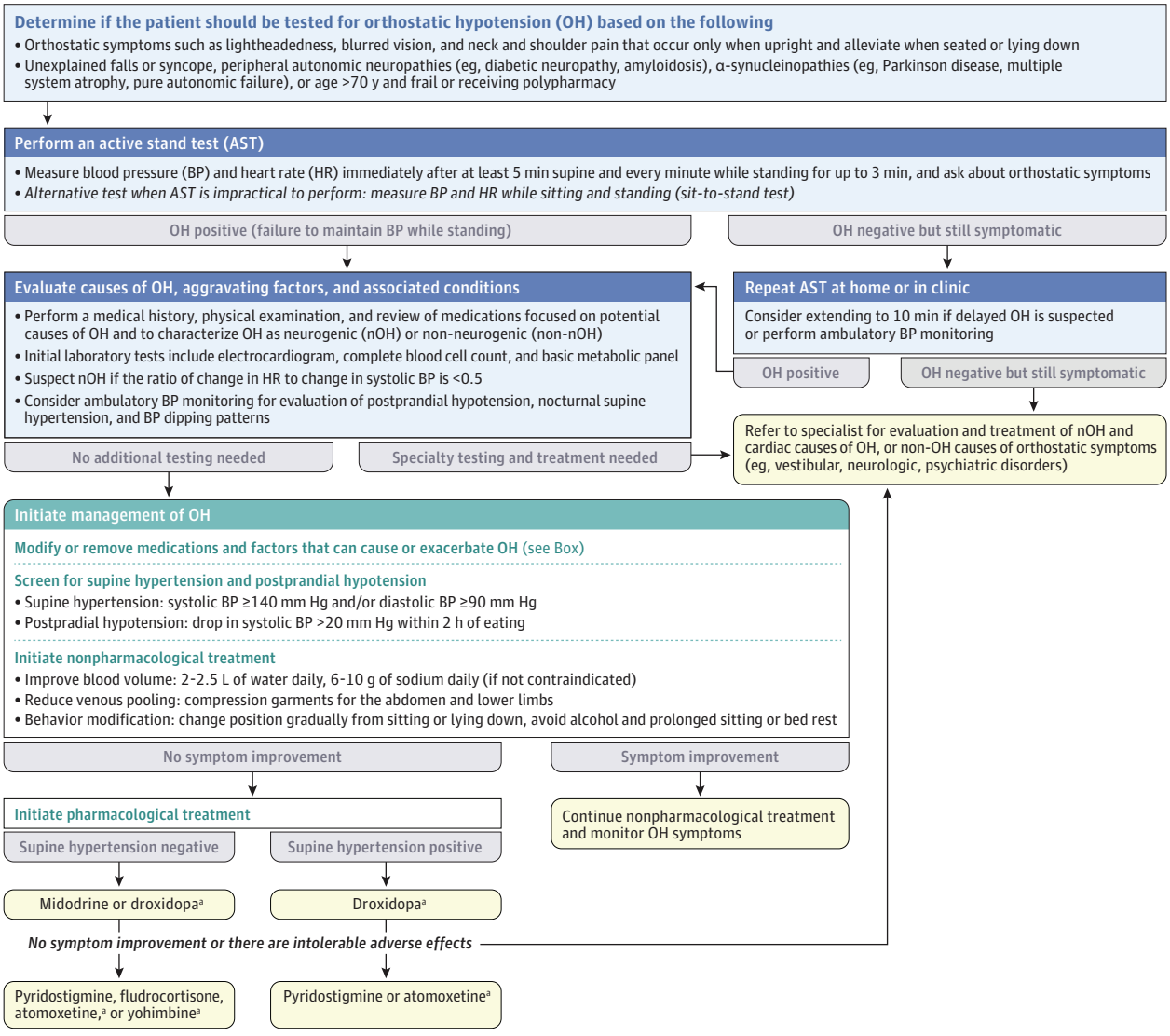
Treatment

Treatment Overview

The goals of OH treatment are to prevent falls, improve orthostatic symptoms, and enhance functional ability. Monitoring the effects

© 2026 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.
Downloaded from jamanetwork.com by guest on 04/07/2026

Figure 2. Diagnostic and Treatment Approach to Orthostatic Hypotension


Determine if the patient should be tested for orthostatic hypotension (OH) based on the following
• Orthostatic symptoms such as lightheadedness, blurred vision, and neck and shoulder pain that occur only when upright and alleviate when seated or lying down
• Unexplained falls or syncope, peripheral autonomic neuropathies (eg, diabetic neuropathy, amyloidosis), α-synucleinopathies (eg, Parkinson disease, multiple system atrophy, pure autonomic failure), or age >70 y and frail or receiving polypharmacy
Perform an active stand test (AST)
• Measure blood pressure (BP) and heart rate (HR) immediately after at least 5 min supine and every minute while standing for up to 3 min, and ask about orthostatic symptoms
• Alternative test when AST is impractical to perform: measure BP and HR while sitting and standing (sit-to-stand test)
OH positive (failure to maintain BP while standing)
OH negative but still symptomatic
Evaluate causes of OH, aggravating factors, and associated conditions
• Perform a medical history, physical examination, and review of medications focused on potential causes of OH and to characterize OH as neurogenic (nOH) or non-neurogenic (non-nOH)
• Initial laboratory tests include electrocardiogram, complete blood cell count, and basic metabolic panel
• Suspect nOH if the ratio of change in HR to change in systolic BP is <0.5
• Consider ambulatory BP monitoring for evaluation of postprandial hypotension, nocturnal supine hypertension, and BP dipping patterns
Repeat AST at home or in clinic
Consider extending to 10 min if delayed OH is suspected or perform ambulatory BP monitoring
OH positive
OH negative but still symptomatic
No additional testing needed
Specialty testing and treatment needed
Refer to specialist for evaluation and treatment of nOH and cardiac causes of OH, or non-OH causes of orthostatic symptoms (eg, vestibular, neurologic, psychiatric disorders)
Initiate management of OH
Modify or remove medications and factors that can cause or exacerbate OH (see Box)
Screen for supine hypertension and postprandial hypotension
• Supine hypertension: systolic BP ≥140 mm Hg and/or diastolic BP ≥90 mm Hg
• Postpradial hypotension: drop in systolic BP >20 mm Hg within 2 h of eating
Initiate nonpharmacological treatment
• Improve blood volume: 2-2.5 L of water daily, 6-10 g of sodium daily (if not contraindicated)
• Reduce venous pooling: compression garments for the abdomen and lower limbs
• Behavior modification: change position gradually from sitting or lying down, avoid alcohol and prolonged sitting or bed rest
No symptom improvement
Symptom improvement
Initiate pharmacological treatment
Continue nonpharmacological treatment and monitor OH symptoms
Supine hypertension negative
Supine hypertension positive
Midodrine or droxidopa[a]
Droxidopa[a]
No symptom improvement or there are intolerable adverse effects
Pyridostigmine, fludrocortisone, atomoxetine,[a] or yohimbine[a]
Pyridostigmine or atomoxetine[a]

[a]Medications that have shown efficacy in studies including only patients with neurogenic orthostatic hypotension.

of treatment on supine and standing BPs can help guide management, but treatment should not aim to reduce the degree of BP drop from supine to standing (ie, OH), as medications often increase BP in both positions.[38,39] Thus, the orthostatic BP drop is often unchanged or even increased in response to treatment.[38,39]

The treatment approach to OH is shown in **Figure 2**. All OH should initially be managed with nonpharmacological measures unless patients are severely symptomatic or at high risk for falls or syncope. The use of most medications for OH is supported by limited evidence of long-term efficacy. Consequently, treatment recommendations are based on small clinical trials, clinical experience, and theoretical pharmacology principles.

Nonpharmacological Treatment

Nonpharmacological measures include removing aggravating factors (Box), improving blood volume, reducing venous pooling, and implementing behavior modification. Patient education is key to the success of these nonpharmacological measures. Patients should understand how posture affects their BP and symptoms, and learn to recognize warning signs of syncope and avoid aggravating factors.

Medication Review

The initial step in managing OH should be a comprehensive review of medications to scrutinize the risks and benefits of any that can cause or exacerbate OH. Cardiovascular and psychotropic drugs, and medications for Parkinson disease or bladder symptoms, are the main culprits. β-Blockers and tricyclic antidepressants can increase the risk of OH by 6- to 7-fold,[40] whereas α-blockers, second-generation antipsychotics, centrally acting antihypertensives, and sodium-glucose cotransporter 2 inhibitors by up to 2-fold.[40] Use of selective serotonin reuptake inhibitors, diuretics, and calcium channel blockers are also associated with OH.[41-43] Discontinuation, dose reduction, or adjusting the dosing schedule of these medications may improve or even resolve OH symptoms. The management of OH and

© 2026 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.
Downloaded from jamanetwork.com by guest on 04/07/2026

coexisting supine or seated hypertension is complex and challenging. The decision to increase or decrease antihypertensives requires careful consideration of the patient's history of hypertension, frailty status, and degree of autonomic impairment.[44] In robust individuals with seated hypertension and OH, treatment with antihypertensives can improve OH (when measured as seated to standing)[45] and cardiovascular outcomes.[46] Older adults with frailty are frequently excluded from hypertension trials, and the harms of treatment, such as hypotension, may be underestimated, so intensification of antihypertensives may not be appropriate.[47] Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are the preferred first-line agents in this scenario, but this is largely based on observational evidence.[44] In patients with nOH and supine hypertension, a permissive supine systolic BP of 160 mm Hg is recommended before starting antihypertensive treatment to prioritize nOH symptom management and fall prevention.[11]

Salt and Water Intake

Patients with any form of OH should drink at least 2 to 2.5 L of water daily to maintain central volume, so long as it is deemed safe in the context of their other medical conditions (eg, congestive heart failure). Patients with autonomic failure have impaired ability to maintain sodium homeostasis[48] and should consume 6 to 10 g of sodium daily via diet or supplements, if not contraindicated.[49,50] In patients with OH, drinking 16 oz (500 mL) of water rapidly (3-4 minutes) can increase BP by 24/12 mm Hg on average.[51] The pressor effect begins after 5 minutes of ingestion, peaks at 35 minutes, and persists for up to 60 minutes.[51] This effect appears to be due to a sympathetic response to the hypoosmolality of water and can be used as a rescue measure to further improve postprandial hypotension and nOH, particularly in the morning.[52] Liquids other than water do not have the same effect.

Reducing Venous Pooling

Compression garments can increase venous return and upright BP by decreasing the venous pooling on standing. Compression of the abdomen and lower limbs, using waist-high compression stockings or a combination of an abdominal binder and whole-leg compression stockings, provides the most effective compression.[53,54] Compression of the abdomen alone is also effective but requires a compression level of 10 to 40 mm Hg.[55,56] Small crossover randomized trials showed that elastic abdominal binders improved both standing systolic BP[54,56-58] and orthostatic symptoms.[54,58] A study using an experimental inflatable abdominal binder during a 10-minute AST showed that abdominal compression alone was as effective as midodrine in improving standing BP, and the combination of both had an additive pressor effect.[59] In contrast, knee-high compression stockings alone have little or no effect because blood pools less in calves.[57] Compression garments, however, are often poorly tolerated due to discomfort and difficulty in donning.[60] Physical countermeasures, such as crossing legs while standing, squatting, and tensing the leg muscles, can reduce venous pooling and be used as a rescue measure.[61,62]

Behavior Modification

Patients with OH should be advised to change position gradually (eg, by moving from lying to sitting and then standing or standing up slowly) to reduce the blood pressure drop on standing.[63] Avoiding alcohol use and prolonged sitting or bed rest can reduce the risk of OH.[64,65] Patients with nOH should be advised to avoid prolonged standing in hot environments, as heat-induced skin vasodilation can exacerbate their symptoms.[66] Sleeping with the bed tilted head up by at least 10° (approximately 13 inches in elevation of the head of the bed) can reduce natriuresis and improve nOH in the mornings, but evidence is weak.[67-70] This can be achieved by placing a wedge under the mattress or blocks under the legs of the bed headboard. Physical therapy may help prevent falls even if OH symptoms persist by improving gait and balance, maintaining mobility to prevent deconditioning, or optimizing use of gait aids, especially in patients with motor symptoms (eg, Parkinson disease and multiple system atrophy).

Pharmacological Treatment

Pressor medications are often necessary when nonpharmacological treatments fail to improve OH symptoms (Figure 2 and **Table**). Medications may also be appropriate as first-line therapy for patients with severe symptoms who are at high risk for falls or syncope. When selecting OH medications, it is important to consider relevant comorbidities (eg, heart failure, chronic kidney disease, diabetes), drug interactions, preexisting hypertension, and, in patients with nOH, the level and severity of the autonomic lesion.[71]

US Food and Drug Administration–Approved Medications

Midodrine is a short-acting α-1 adrenoceptor agonist (half-life of 3-4 hours) that has been shown to improve standing systolic BP and orthostatic symptoms compared to placebo,[72-74] with an effect that persisted at 6 months of treatment.[75] It is the only US Food and Drug Administration–approved drug for both nOH and non-nOH and is thus considered the first-line treatment (Figure 2). Common adverse effects include scalp pruritus, urinary retention, and supine hypertension, which can be minimized by taking the evening dose earlier or skipping it.[76]

Droxidopa, a US Food and Drug Administration–approved norepinephrine prodrug for nOH, improves standing BP, orthostatic symptoms, and activities of daily living in patients with autonomic failure.[77] No trials have directly compared droxidopa to midodrine; however, a meta-analysis found that midodrine was more likely to cause supine hypertension.[78] Droxidopa also appears to be better tolerated (eg, no urinary retention has been reported),[79] but higher doses may be required in patients taking dopa decarboxylase inhibitors.[77] Adverse effects include headache, dizziness, nausea, and supine hypertension. Both midodrine and droxidopa are first-line treatments for nOH, but droxidopa is preferred in patients with higher supine BPs due to its lower risk of supine hypertension (Figure 2).

Off-Label Medications

Medications used off label for the treatment of OH are considered second-line treatments and can be used in addition to midodrine or droxidopa when symptoms persist with maximum doses or as alternatives if they are poorly tolerated (Figure 2). Fludrocortisone is a synthetic mineralocorticoid that has been used to treat OH for more than 40 years. It increases kidney sodium reabsorption and expands plasma volume. However, this effect is transient, and its long-term benefit may result from enhancing the pressor effects of norepinephrine and angiotensin II.[80,81] A 2021 Cochrane review, however, found very low-certainty evidence of benefit from 3 small

© 2026 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.
Downloaded from jamanetwork.com by guest on 04/07/2026

Table. Pharmacologic Treatment Options for Orthostatic Hypotension and Postprandial Hypotension

Medication	Mechanism of action	Dosage	Contraindications	Common adverse events
Midodrine	α-1 Adrenergic agonist	Oral: 2.5-10 mg, 1-3 times daily (avoid ≤5 h before bedtime)	Severe cardiovascular disease, urinary retention, acute kidney failure, pheochromocytoma	Supine hypertension, piloerection, scalp pruritus, urinary retention
Droxidopa	Synthetic norepinephrine precursor	Oral: 100-600 mg, 2-3 times daily (avoid ≤3 h before bedtime)	Concomitant use of nonselective monoamine oxidase inhibitors due to risk of hypertension	Headache, dizziness, nausea, fatigue and supine hypertension; hyperpyrexia and confusion are rare
Fludrocortisone	Synthetic mineralocorticoid; transient effect: sodium retention and plasma volume expansion; long-term effect: potentiation of norepinephrine and angiotensin II	Oral: 0.05-0.2 mg daily	Systemic fungal infections, heart failure	Supine hypertension, hypokalemia, fluid retention, headache and edema; check electrolytes 1 wk after initiation
Atomoxetine	Norepinephrine reuptake inhibitor; increases synaptic norepinephrine levels	Oral: 10 or 18 mg 1-3 times daily (avoid ≤5 h before bedtime)	Narrow-angle glaucoma, severe cardiovascular disorders, monoamine oxidase inhibitor use within 14 d	Nausea, dry mouth, insomnia, increased heart rate, supine hypertension, urinary retention
Pyridostigmine	Acetylcholinesterase inhibitor; enhances autonomic ganglia transmission	Oral: 30-60 mg, 1-3 times daily	Gastrointestinal or urinary obstruction, asthma	Excessive salivation or sweating, urinary incontinence, abdominal cramps, diarrhea, bradycardia
Yohimbine	α-2 Adrenergic antagonist; increases norepinephrine release	Oral: 5.4 mg, 1-3 times daily (avoid ≤5 h before bedtime)	Severe kidney or hepatic impairment, anxiety, psychosis, or taking monoamine oxidase inhibitors, tricyclic antidepressants, and other sympathomimetics	Anxiety, tachycardia, dizziness abdominal discomfort
Octreotide	Somatostatin analog; reduces splanchnic vasodilation and increases peripheral resistance	Subcutaneous: 12.5-25 μg, 1-3 times daily (avoid ≤5 h before bedtime); postprandial hypotension: 20 min before meals	Severe liver or kidney impairment	Cholelithiasis, arrhythmias, hyperglycemia and hypoglycemia, hypothyroidism
Caffeine	Adenosine receptor antagonist	Oral: 100-250 mg, 15-30 min before meals	Severe cardiac arrhythmias, peptic ulcer disease	Insomnia, palpitations, gastrointestinal irritation, anxiety
Acarbose	α-Glucosidase inhibitor; slows carbohydrate absorption, reducing postprandial blood pressure drop	Oral: 50-100 mg, 20-30 min before meals	Inflammatory bowel disease, intestinal obstruction, diabetic ketoacidosis	Flatulence, diarrhea, abdominal discomfort, bloating, pneumatosis cystoides intestinalis

randomized trials showing improvements in orthostatic systolic BP and symptoms in a total of 28 participants studied for up to 3 weeks.[82] Adverse effects include supine hypertension, hypokalemia, edema, and acute decompensation in patients with heart failure, and it is poorly tolerated at 1 year.[83-85] Compared with midodrine, fludrocortisone has been shown to increase all-cause hospitalization in patients with OH,[83] and it should not be used in patients with hypertension or congestive heart failure.

Atomoxetine is a norepinephrine transporter inhibitor approved for attention-deficit hyperactivity disorder. Single-dose trials in patients with autonomic failure showed that atomoxetine improved standing BP and nOH symptoms, even at pediatric doses, by decreasing norepinephrine reuptake in postganglionic sympathetic nerves.[86] The pressor effects are greater in patients with residual sympathetic function, such as those with multiple system atrophy.[86,87] Compared with midodrine, atomoxetine appears superior in improving standing BP and orthostatic symptoms, despite having similar pressor effects while seated.[87] However, a recent randomized trial in patients with multiple system atrophy showed that the initial pressor effects of atomoxetine observed at 2 weeks did not persist at 1 month, possibly due to tachyphylaxis.[88] Adverse effects include dry mouth, insomnia, supine hypertension, increased heart rate, and suicidal ideation.

Pyridostigmine, an acetylcholinesterase inhibitor approved for myasthenia gravis, increases BP in patients with nOH by facilitating cholinergic transmission in the autonomic ganglia and enhancing residual sympathetic tone. Pyridostigmine is less potent than midodrine[75] or fludrocortisone,[89] but it has the advantage that its pressor effects are greater on standing compared to lying down because of the sympathetic activation on standing.[90,91] Pyridostigmine is more effective in individuals with milder autonomic impairment (ie, higher residual sympathetic tone) and those without supine hypertension (also a marker of autonomic failure severity).[91-93] Thus, it can be useful in older patients with apparent non-nOH, given that aging is associated with decreased baroreflex sensitivity.[94,95] In severe nOH, pyridostigmine appears to have a synergistic effect with atomoxetine.[96] Adverse effects include sialorrhea, sweating, urinary incontinence, abdominal cramps, and diarrhea. This latter adverse effect can benefit patients with autonomic failure who often experience severe constipation.

Yohimbine, an α-2 adrenergic antagonist, improves standing BP and orthostatic symptoms in patients with autonomic failure by enhancing central sympathetic tone.[92] In patients with peripheral autonomic failure who did not respond to yohimbine or atomoxetine alone, the combination showed synergistic pressor effects.[96,97] However, these trials tested the effects of a single dose; the long-term efficacy and safety of yohimbine are unknown. Yohimbine is no longer available on the market; it can only be obtained through a compounding pharmacy or as part of herbal supplements. Due to its potential serious adverse effects (eg, arrhythmias, seizures) and interactions with medications, including monoamine oxidase inhibitors, tricyclic antidepressants, and those metabolized by CYP2D6 and CYP3A, its use should be deferred to the autonomic specialist.

Octreotide can produce a potent pressor effect in patients with autonomic failure by constricting the splanchnic vasculature.[98-100] It could be an alternative when other medications fail. However, its

© 2026 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.
Downloaded from jamanetwork.com by guest on 04/07/2026

use is limited by the need for parenteral administration and gastrointestinal adverse effects.

Treatment of Postprandial Hypotension

Nonpharmacological approaches may be sufficient to treat mild postprandial hypotension, such as eating smaller, more frequent meals (eg, 6 smaller meals per day instead of 3 larger ones) and reducing carbohydrate intake, particularly simple carbohydrates.[101,102] Caffeine and water boluses with meals can also reduce postprandial hypotension.[103,104]

Pharmacological interventions can be added in more severe cases or as needed when a larger meal is anticipated. Acarbose, given 20-30 minutes before meals, improved postprandial hypotension by 13 to 27 mm Hg in patients with autonomic failure and older adults.[105,106] It can cause bloating and loose stools, so slow titration is advised. Octreotide can also improve postprandial hypotension by reducing gastrointestinal and pancreatic hormone release.[99,107,108]

Treatment of OH in Patients With Supine Hypertension

Fludrocortisone, midodrine, and other long-acting pressor drugs should be avoided in patients with OH and supine hypertension. Short-acting drugs are preferred, and omitting evening doses may help manage nocturnal supine hypertension. The first-line treatment should be droxidopa because of its lower risk of supine hypertension (Figure 2). Second-line options include atomoxetine and pyridostigmine, as they also have a lower risk of supine hypertension since they enhance residual sympathetic activation (eg, when standing) rather than directly stimulating adrenoreceptors. Pyridostigmine, however, has been found to be less effective in patients with hypertension.[93]

Supine hypertension can be managed with nonpharmacological measures. During the day, the most effective way to treat supine hypertension without worsening OH is to avoid the supine position, particularly after taking pressor drugs. During the night, sleeping with the bed tilted head up by 10° or more may reduce supine hypertension and nocturia, and improve morning OH. A carbohydrate-rich snack before bedtime can also transiently lower BP by taking advantage of the coexistent postprandial hypotension in patients with autonomic failure.[109] In patients with seated hypertension during the day, antihypertensives with short half-lives, such as angiotensin II receptor blockers (eg, losartan) or calcium channel blockers, might be considered.[110] In patients with nocturnal supine hypertension (despite nonpharmacological treatment), short-acting antihypertensive drugs can be given at bedtime (eg, nitroglycerin patch, losartan, nebivolol, eplerenone).[69,110] However, none of the antihypertensives tested has been shown to improve morning OH.[44] Preliminary studies with continuous positive airway pressure or a heated mattress suggest that these interventions can reduce nocturnal BP and diuresis and improve morning OH in patients with autonomic failure and supine hypertension.[66,111]

Conclusions

OH is a common and often disabling condition, particularly in older individuals and those with autonomic dysfunction. Primary care physicians often play an important role in the evaluation and treatment of OH. Treatment requires a combination of nonpharmacological strategies, such as medication review, increased fluid and salt intake, and compression garments, as well as pharmacological therapies tailored to the underlying cause and comorbidities. Individualized treatment, regular monitoring, and patient education are essential to improve symptoms, prevent falls, and enhance quality of life. Despite limited long-term evidence for most therapies, a patient-centered, stepwise approach remains the cornerstone of care. Ongoing research is needed to optimize management and outcomes for patients with OH.

ARTICLE INFORMATION

Accepted for Publication: January 29, 2026.

Published Online: April 6, 2026. doi:10.1001/jamainternmed.2026.0284

Conflict of Interest Disclosures: Dr Okamoto reported grants from the National Institutes of Health/National Center for Advancing Translational Sciences during the conduct of the study; in addition, Dr Okamoto had a patent issued for the use of an automated inflatable abdominal binder as a medical device for the treatment of orthostatic hypotension. No other disclosures were reported.

Funding/Support: Dr Okamoto was supported by grants from the National Institutes of Health (HL144568, RO1 HL161095) and the Clinical and Translational Science Awards Program (UL1 TR002243) from the National Center for Advancing Translational Sciences.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The contents of this work are solely the responsibility of the authors and do not necessarily represent the official views of the National Center for Advancing Translational Sciences or the National Institutes of Health.

REFERENCES

1. Saedon NI, Pin Tan M, Frith J. The prevalence of orthostatic hypotension: a systematic review and meta-analysis. *J Gerontol A Biol Sci Med Sci*. 2020;75(1):117-122. doi:10.1093/gerona/gly188

2. Ricci F, De Caterina R, Fedorowski A. Orthostatic hypotension: epidemiology, prognosis, and treatment. *J Am Coll Cardiol*. 2015;66(7):848-860. doi:10.1016/j.jacc.2015.06.1084

3. McDonagh STJ, Mejzner N, Clark CE. Prevalence of postural hypotension in primary, community and institutional care: a systematic review and meta-analysis. *BMC Fam Pract*. 2021;22(1):1. doi:10.1186/s12875-020-01313-8

4. Merola A, Romagnolo A, Rosso M, et al. Autonomic dysfunction in Parkinson's disease: a prospective cohort study. *Mov Disord*. 2018;33(3):391-397. doi:10.1002/mds.27268

5. Juraschek SP, Daya N, Rawlings AM, et al. Association of history of dizziness and long-term adverse outcomes with early vs later orthostatic hypotension assessment times in middle-aged adults. *JAMA Intern Med*. 2017;177(9):1316-1323. doi:10.1001/jamainternmed.2017.2937

6. Doyle K, Lavan A, Kenny RA, Briggs R. Delayed blood pressure recovery after standing independently predicts fracture in community-dwelling older people. *J Am Med Dir Assoc*. 2021;22(6):1235-1241.e1. doi:10.1016/j.jamda.2020.12.031

7. Angelousi A, Girerd N, Benetos A, et al. Association between orthostatic hypotension and cardiovascular risk, cerebrovascular risk, cognitive decline and falls as well as overall mortality: a systematic review and meta-analysis. *J Hypertens*. 2014;32(8):1562-1571. doi:10.1097/HJH.0000000000000235

8. Claffey P, Pérez-Denia L, Lavan A, Kenny RA, Finucane C, Briggs R. Asymptomatic orthostatic hypotension and risk of falls in community-dwelling older people. *Age Ageing*. 2022;51(12):afac295. doi:10.1093/ageing/afac295

© 2026 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by guest on 04/07/2026

9. Magkas N, Tsioufis C, Thomopoulos C, et al. Orthostatic hypotension: from pathophysiology to clinical applications and therapeutic considerations. *J Clin Hypertens (Greenwich)*. 2019;21(5):546-554. doi:10.1111/jch.13521

10. Freeman R, Wieling W, Axelrod FB, et al. Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome. *Clin Auton Res*. 2011;21(2):69-72. doi:10.1007/s10286-011-0119-5

11. Gibbons CH, Schmidt P, Biaggioni I, et al. The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension. *J Neurol*. 2017;264(8):1567-1582. doi:10.1007/s00415-016-8375-x

12. Torabi P, Ricci F, Hamrefors V, Sutton R, Fedorowski A. Classical and delayed orthostatic hypotension in patients with unexplained syncope and severe orthostatic intolerance. *Front Cardiovasc Med*. 2020;7:21. doi:10.3389/fcvm.2020.00021

13. Gibbons CH, Freeman R. Clinical implications of delayed orthostatic hypotension: a 10-year follow-up study. *Neurology*. 2015;85(16):1362-1367. doi:10.1212/WNL.0000000000002030

14. Biaggioni I. All orthostatic hypotension is neurogenic. *Clin Auton Res*. 2023;33(4):383-386. doi:10.1007/s10286-023-00966-6

15. Johansson M, Gagaouzova BS, van Rossum IA, et al. Aetiology and haemodynamic patterns of orthostatic hypotension in a tertiary syncope unit. *Europace*. 2025;27(5):euaf017. doi:10.1093/europace/euaf017

16. Gagaouzova BS, van der Stam A, Johansson M, et al. The relative contribution of hemodynamic parameters to blood pressure decrease in classical orthostatic hypotension. *J Hypertens*. 2025;43(3):436-444. doi:10.1097/HJH.0000000000003832

17. Montero-Odasso M, van der Velde N, Martin FC, et al; Task Force on Global Guidelines for Falls in Older Adults. World guidelines for falls prevention and management for older adults: a global initiative. *Age Ageing*. 2022;51(9):afac205. doi:10.1093/ageing/afac205

18. Ward C, Kenny RA. Reproducibility of orthostatic hypotension in symptomatic elderly. *Am J Med*. 1996;100(4):418-422. doi:10.1016/S0002-9343(97)89517-4

19. Finucane C, van Wijnen VK, Fan CW, et al. A practical guide to active stand testing and analysis using continuous beat-to-beat non-invasive blood pressure monitoring. *Clin Auton Res*. 2019;29(4):427-441. doi:10.1007/s10286-019-00606-y

20. Norcliffe-Kaufmann L, Kaufmann H, Palma JA, et al; Autonomic Disorders Consortium. Orthostatic heart rate changes in patients with autonomic failure caused by neurodegenerative synucleinopathies. *Ann Neurol*. 2018;83(3):522-531. doi:10.1002/ana.25170

21. Cremer A, Rousseau AL, Boulestreau R, Kuntz S, Tzourio C, Gosse P. Screening for orthostatic hypotension using home blood pressure measurements. *J Hypertens*. 2019;37(5):923-927. doi:10.1097/HJH.0000000000001986

22. Gibbon JR, Parry SW, Witham MD, Yarnall A, Frith J. Feasibility, reliability and safety of self-assessed orthostatic blood pressure at home. *Age Ageing*. 2022;51(7):afac153. doi:10.1093/ageing/afac153

23. Cohen A, Vidal JS, Roca F, et al. Feasibility and determinants of orthostatic hypotension self-measurement at home in an elderly community-dwelling population. *Am J Hypertens*. 2019;32(9):824-832. doi:10.1093/ajh/hpz066

24. Finucane C, Savva GM, Kenny RA. Reliability of orthostatic beat-to-beat blood pressure tests: implications for population and clinical studies. *Clin Auton Res*. 2017;27(1):31-39. doi:10.1007/s10286-016-0393-3

25. Shaw BH, Garland EM, Black BK, et al. Optimal diagnostic thresholds for diagnosis of orthostatic hypotension with a 'sit-to-stand test'. *J Hypertens*. 2017;35(5):1019-1025. doi:10.1097/HJH.0000000000001265

26. Aydin AE, Soysal P, Isik AT. Which is preferable for orthostatic hypotension diagnosis in older adults: active standing test or head-up tilt table test? *Clin Interv Aging*. 2017;12:207-212. doi:10.2147/CIA.S129868

27. Grobman B, Turkson-Ocran RN, Staessen JA, et al. Body position and orthostatic hypotension in hypertensive adults: results from the Syst-Eur Trial. *Hypertension*. 2023;80(4):820-827. doi:10.1161/HYPERTENSIONAHA.122.20602

28. Cooke J, Carew S, O'Connor M, Costelloe A, Sheehy T, Lyons D. Sitting and standing blood pressure measurements are not accurate for the diagnosis of orthostatic hypotension. *QJM*. 2009;102(5):335-339. doi:10.1093/qjmed/hcp020

29. Gabriele S, Georgiopoulos I, Labat C, et al. Can sitting and lying blood pressure measurements be considered interchangeable in older frail adults? *Eur Geriatr Med*. 2022;13(6):1407-1415. doi:10.1007/s41999-022-00669-7

30. Juraschek SP, Appel LJM, M Mitchell C, et al. Comparison of supine and seated orthostatic hypotension assessments and their association with falls and orthostatic symptoms. *J Am Geriatr Soc*. 2022;70(8):2310-2319. doi:10.1111/jgs.17804

31. Lamotte G, Coon EA, Suarez MD, et al. Standardized autonomic testing in patients with probable radiation-induced afferent baroreflex failure. *Hypertension*. 2022;79(1):50-56. doi:10.1161/HYPERTENSIONAHA.121.17805

32. Shannon J, Jordan J, Costa F, Robertson RM, Biaggioni I. The hypertension of autonomic failure and its treatment. *Hypertension*. 1997;30(5):1062-1067. doi:10.1161/01.HYP.30.5.1062

33. Jansen RW, Lipsitz LA. Postprandial hypotension: epidemiology, pathophysiology, and clinical management. *Ann Intern Med*. 1995;122(4):286-295. doi:10.7326/0003-4819-122-4-199502150-00009

34. Lei LY, Chew DS, Raj SR. Differential diagnosis of orthostatic hypotension. *Auton Neurosci*. 2020;228:102713. doi:10.1016/j.autneu.2020.102713

35. Norcliffe-Kaufmann L, Kaufmann H. Is ambulatory blood pressure monitoring useful in patients with chronic autonomic failure? *Clin Auton Res*. 2014;24(4):189-192. doi:10.1007/s10286-014-0229-y

36. Jansen RWMM. Postprandial hypotension: simple treatment but difficulties with the diagnosis. *J Gerontol A Biol Sci Med Sci*. 2005;60(10):1268-1270. doi:10.1093/gerona/60.10.1268

37. Awosika A, Adabanya U, Millis RM, Omole AE, Moon JH. Postprandial hypotension: an underreported silent killer in the aged. *Cureus*. 2023;15(2):e35411. doi:10.7759/cureus.35411

38. Baker JR, Beach PA, Ranada SI, et al. Cerebral blood flow dynamics in neurogenic orthostatic hypotension: a systematic review and meta-analysis. *Hypertension*. 2025;82(1):106-117. doi:10.1161/HYPERTENSIONAHA.124.23188

39. Freeman R, Illigens BMW, Lapusca R, et al. Symptom recognition is impaired in patients with orthostatic hypotension. *Hypertension*. 2020;75(5):1325-1332. doi:10.1161/HYPERTENSIONAHA.119.13619

40. Bhanu C, Nimmons D, Petersen I, et al. Drug-induced orthostatic hypotension: a systematic review and meta-analysis of randomised controlled trials. *PLoS Med*. 2021;18(11):e1003821. doi:10.1371/journal.pmed.1003821

41. Rivasi G, Rafanelli M, Mossello E, Brignole M, Ungar A. Drug-related orthostatic hypotension: beyond anti-hypertensive medications. *Drugs Aging*. 2020;37(10):725-738. doi:10.1007/s40266-020-00796-5

42. Moonen JEF, Foster-Dingley JC, de Ruijter W, van der Grond J, de Craen AJM, van der Mast RC. Effect of discontinuation of antihypertensive medication on orthostatic hypotension in older persons with mild cognitive impairment: the DANTE Study Leiden. *Age Ageing*. 2016;45(2):249-255. doi:10.1093/ageing/afv199

43. Fotherby MD, Potter JF. Orthostatic hypotension and anti-hypertensive therapy in the elderly. *Postgrad Med J*. 1994;70(830):878-881. doi:10.1136/pgmj.70.830.878

44. Juraschek SP, Cortez MM, Flack JM, et al; American Heart Association Council on Hypertension. Orthostatic hypotension in adults with hypertension: a scientific statement from the American Heart Association. *Hypertension*. 2024;81(3):e16-e30. doi:10.1161/HYP.0000000000000236

45. Juraschek SP, Hu JR, Cluett JL, et al. Effects of intensive blood pressure treatment on orthostatic hypotension: a systematic review and individual participant-based meta-analysis. *Ann Intern Med*. 2021;174(1):58-68. doi:10.7326/M20-4298

46. Juraschek SP, Hu JR, Cluett JL, et al. Orthostatic hypotension, hypertension treatment, and cardiovascular disease: an individual participant meta-analysis. *JAMA*. 2023;330(15):1459-1471. doi:10.1001/jama.2023.18497

47. Sexton DJ, Canney M, O'Connell MDL, et al. Injurious falls and syncope in older community-dwelling adults meeting inclusion criteria for SPRINT. *JAMA Intern Med*. 2017;177(9):1385-1387. doi:10.1001/jamainternmed.2017.2924

48. Biaggioni I. Blood pressure regulation in autonomic failure by dietary sodium, blood volume and posture. *Auton Neurosci*. 2021;236:102891. doi:10.1016/j.autneu.2021.102891

49. Brignole M, Moya A, de Lange FJ, et al; ESC Scientific Document Group. 2018 ESC Guidelines for the diagnosis and management of syncope. *Eur Heart J*. 2018;39(21):1883-1948. doi:10.1093/eurheartj/ehy037

50. Shen WK, Sheldon RS, Benditt DG, et al; Writing Committee Members. 2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: a report of the American College of Cardiology/American Heart Association

© 2026 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by guest on 04/07/2026

Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Heart Rhythm*. 2017;14(8):e155-e217. doi:10.1016/j.hrthm.2017.03.004

51. Jordan J, Shannon JR, Black BK, et al. The pressor response to water drinking in humans: a sympathetic reflex? *Circulation*. 2000;101(5):504-509. doi:10.1161/01.CIR.101.5.504

52. May M, Jordan J. The osmopressor response to water drinking. *Am J Physiol Regul Integr Comp Physiol*. 2011;300(1):R40-R46. doi:10.1152/ajpregu.00544.2010

53. Denq JC, Opfer-Gehrking TL, Giuliani M, Felten J, Convertino VA, Low PA. Efficacy of compression of different capacitance beds in the amelioration of orthostatic hypotension. *Clin Auton Res*. 1997;7(6):321-326. doi:10.1007/BF02267725

54. Podoleanu C, Maggi R, Brignole M, et al. Lower limb and abdominal compression bandages prevent progressive orthostatic hypotension in elderly persons: a randomized single-blind controlled study. *J Am Coll Cardiol*. 2006;48(7):1425-1432. doi:10.1016/j.jacc.2006.06.052

55. Smit AAJ, Wieling W, Fujimura J, et al. Use of lower abdominal compression to combat orthostatic hypotension in patients with autonomic dysfunction. *Clin Auton Res*. 2004;14(3):167-175. doi:10.1007/s10286-004-0187-x

56. Figueroa JJ, Singer W, Sandroni P, et al. Effects of patient-controlled abdominal compression on standing systolic blood pressure in adults with orthostatic hypotension. *Arch Phys Med Rehabil*. 2015;96(3):505-510. doi:10.1016/j.apmr.2014.10.012

57. Newton JL, Frith J. The efficacy of nonpharmacologic intervention for orthostatic hypotension associated with aging. *Neurology*. 2018;91(7):e652-e656. doi:10.1212/WNL.0000000000005994

58. Fanciulli A, Goebel G, Metzler B, et al. Elastic abdominal binders attenuate orthostatic hypotension in Parkinson's disease. *Mov Disord Clin Pract*. 2015;3(2):156-160. doi:10.1002/mdc3.12270

59. Okamoto LE, Diedrich A, Baudenbacher FJ, et al. Efficacy of servo-controlled splanchnic venous compression in the treatment of orthostatic hypotension: a randomized comparison with midodrine. *Hypertension*. 2016;68(2):418-426. doi:10.1161/HYPERTENSIONAHA.116.07199

60. Mitra K, Kunte S, Taube S, et al. Current landscape of compression products for treatment of postural orthostatic tachycardia syndrome and neurogenic orthostatic hypotension. *J Clin Med*. 2024;13(23):7304. doi:10.3390/jcm13237304

61. Sheikh NA, Ranada S, Lloyd M, et al. Lower body muscle preactivation and tensing mitigate symptoms of initial orthostatic hypotension in young females. *Heart Rhythm*. 2022;19(4):604-610. doi:10.1016/j.hrthm.2021.12.030

62. Bouvette CM, McPhee BR, Opfer-Gehrking TL, Low PA. Role of physical countermaneuvers in the management of orthostatic hypotension: efficacy and biofeedback augmentation. *Mayo Clin Proc*. 1996;71(9):847-853. doi:10.4065/71.9.847

63. de Bruïne ES, Reijnierse EM, Trappenburg MC, et al. Standing up slowly antagonises initial blood pressure decrease in older adults with orthostatic hypotension. *Gerontology*. 2017;63(2):137-143. doi:10.1159/000450642

64. Kamiya A, Michikami D, Fu Q, et al. Pathophysiology of orthostatic hypotension after bed rest: paradoxical sympathetic withdrawal. *Am J Physiol Heart Circ Physiol*. 2003;285(3):H1158-H1167. doi:10.1152/ajpheart.00965.2002

65. Narkiewicz K, Cooley RL, Somers VK. Alcohol potentiates orthostatic hypotension: implications for alcohol-related syncope. *Circulation*. 2000;101(4):398-402. doi:10.1161/01.CIR.101.4.398

66. Okamoto LE, Celedonio JE, Smith EC, et al. Local passive heat for the treatment of hypertension in autonomic failure. *J Am Heart Assoc*. 2021;10(7):e018979. doi:10.1161/JAHA.120.018979

67. van der Stam AH, Shmuely S, de Vries NM, Bloem BR, Thijs RD. The impact of head-up tilt sleeping on orthostatic tolerance: a scoping review. *Biology (Basel)*. 2023;12(8):1108. doi:10.3390/biology12081108

68. Jordan J, Fanciulli A, Tank J, et al. Management of supine hypertension in patients with neurogenic orthostatic hypotension: scientific statement of the American Autonomic Society, European Federation of Autonomic Societies, and the European Society of Hypertension. *J Hypertens*. 2019;37(8):1541-1546. doi:10.1097/HJH.0000000000002078

69. Fanciulli A, Jordan J, Biaggioni I, et al. Consensus statement on the definition of neurogenic supine hypertension in cardiovascular autonomic failure by the American Autonomic Society (AAS) and the European Federation of Autonomic Societies (EFAS): endorsed by the European Academy of Neurology (EAN) and the European Society of Hypertension (ESH). *Clin Auton Res*. 2018;28(4):355-362. doi:10.1007/s10286-018-0529-8

70. van Lieshout JJ, ten Harkel AD, Wieling W. Fludrocortisone and sleeping in the head-up position limit the postural decrease in cardiac output in autonomic failure. *Clin Auton Res*. 2000;10(1):35-42. doi:10.1007/BF02291388

71. Benarroch EE. The clinical approach to autonomic failure in neurological disorders. *Nat Rev Neurol*. 2014;10(7):396-407. doi:10.1038/nrneurol.2014.88

72. Wright RA, Kaufmann HC, Perera R, et al. A double-blind, dose-response study of midodrine in neurogenic orthostatic hypotension. *Neurology*. 1998;51(1):120-124. doi:10.1212/WNL.51.1.120

73. Jankovic J, Gilden JL, Hiner BC, et al. Neurogenic orthostatic hypotension: a double-blind, placebo-controlled study with midodrine. *Am J Med*. 1993;95(1):38-48. doi:10.1016/0002-9343(93)90230-M

74. Fouad-Tarazi FM, Okabe M, Goren H. Alpha sympathomimetic treatment of autonomic insufficiency with orthostatic hypotension. *Am J Med*. 1995;99(6):604-610. doi:10.1016/S0002-9343(99)80246-0

75. Byun JI, Moon J, Kim DY, et al. Efficacy of single or combined midodrine and pyridostigmine in orthostatic hypotension. *Neurology*. 2017;89(10):1078-1086. doi:10.1212/WNL.0000000000004340

76. Young TM, Mathias CJ. Taste and smell disturbance with the alpha-adrenoceptor agonist midodrine. *Ann Pharmacother*. 2004;38(11):1868-1870. doi:10.1345/aph.1E171

77. Biaggioni I, Arthur Hewitt L, Rowse GJ, Kaufmann H. Integrated analysis of droxidopa trials for neurogenic orthostatic hypotension. *BMC Neurol*. 2017;17(1):90. doi:10.1186/s12883-017-0867-5

78. Chen JJ, Han Y, Tang J, Portillo I, Hauser RA, Dashtipour K. Standing and supine blood pressure outcomes associated with droxidopa and midodrine in patients with neurogenic orthostatic hypotension: a bayesian meta-analysis and mixed treatment comparison of randomized trials. *Ann Pharmacother*. 2018;52(12):1182-1194. doi:10.1177/1060028018786954

79. Kymes SM, Sullivan C, Jackson K, Raj SR. Real-world droxidopa or midodrine treatment persistence in patients with neurogenic orthostatic hypotension or orthostatic hypotension. *Auton Neurosci*. 2020;225:102659. doi:10.1016/j.autneu.2020.102659

80. Ten Harkel AD, Van Lieshout JJ, Wieling W. Treatment of orthostatic hypotension with sleeping in the head-up tilt position, alone and in combination with fludrocortisone. *J Intern Med*. 1992;232(2):139-145. doi:10.1111/j.1365-2796.1992.tb00563.x

81. Hickler RB, Thompson GR, Fox LM, Hamlin JT III. Successful treatment of orthostatic hypotension with 9-alpha-fluorohydrocortisone. *N Engl J Med*. 1959;261(16):788-791. doi:10.1056/NEJM195910152611604

82. Veazie S, Peterson K, Ansari Y, et al. Fludrocortisone for orthostatic hypotension. *Cochrane Database Syst Rev*. 2021;5(5):CD012868. doi:10.1002/14651858.CD012868.pub2

83. Grijalva CG, Biaggioni I, Griffin MR, Shibao CA. Fludrocortisone is associated with a higher risk of all-cause hospitalizations compared with midodrine in patients with orthostatic hypotension. *J Am Heart Assoc*. 2017;6(10):e006848. doi:10.1161/JAHA.117.006848

84. Hussain RM, McIntosh SJ, Lawson J, Kenny RA. Fludrocortisone in the treatment of hypotensive disorders in the elderly. *Heart*. 1996;76(6):507-509. doi:10.1136/hrt.76.6.507

85. Shibao C, Grijalva CG, Lipsitz LA, Biaggioni I, Griffin MR. Early discontinuation of treatment in patients with orthostatic hypotension. *Auton Neurosci*. 2013;177(2):291-296. doi:10.1016/j.autneu.2013.08.064

86. Shibao C, Raj SR, Gamboa A, et al. Norepinephrine transporter blockade with atomoxetine induces hypertension in patients with impaired autonomic function. *Hypertension*. 2007;50(1):47-53. doi:10.1161/HYPERTENSIONAHA.107.089961

87. Ramirez CE, Okamoto LE, Arnold AC, et al. Efficacy of atomoxetine versus midodrine for the treatment of orthostatic hypotension in autonomic failure. *Hypertension*. 2014;64(6):1235-1240. doi:10.1161/HYPERTENSIONAHA.114.04225

88. Mwesigwa N, Millar Vernetti P, Kirabo A, et al. Atomoxetine on neurogenic orthostatic hypotension: a randomized, double-blind, placebo-controlled crossover trial. *Clin Auton Res*. 2024;34(6):561-569. doi:10.1007/s10286-024-01051-2

89. Schreglmann SR, Büchele F, Sommerauer M, et al. Pyridostigmine bromide versus fludrocortisone in the treatment of orthostatic hypotension in Parkinson's disease—a randomized controlled trial. *Eur J Neurol*. 2017;24(4):545-551. doi:10.1111/ene.13260

90. Singer W, Opfer-Gehrking TL, McPhee BR, Hilz MJ, Bharucha AE, Low PA. Acetylcholinesterase

© 2026 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by guest on 04/07/2026

inhibition: a novel approach in the treatment of neurogenic orthostatic hypotension. *J Neurol Neurosurg Psychiatry*. 2003;74(9):1294-1298. doi:10.1136/jnnp.74.9.1294

91. Singer W, Sandroni P, Opfer-Gehrking TL, et al. Pyridostigmine treatment trial in neurogenic orthostatic hypotension. *Arch Neurol*. 2006;63(4):513-518. doi:10.1001/archneur.63.4.noc50340

92. Shibao C, Okamoto LE, Gamboa A, et al. Comparative efficacy of yohimbine against pyridostigmine for the treatment of orthostatic hypotension in autonomic failure. *Hypertension*. 2010;56(5):847-851. doi:10.1161/HYPERTENSIONAHA.110.154898

93. Okamoto LE, Walsh E, Diedrich A, et al. Clinical correlates of efficacy of pyridostigmine in the treatment of orthostatic hypotension. *Hypertension*. 2025;82(3):489-497. doi:10.1161/HYPERTENSIONAHA.124.24050

94. Monahan KD. Effect of aging on baroreflex function in humans. *Am J Physiol Regul Integr Comp Physiol*. 2007;293(1):R3-R12. doi:10.1152/ajpregu.00031.2007

95. Jones PP, Christou DD, Jordan J, Seals DR. Baroreflex buffering is reduced with age in healthy men. *Circulation*. 2003;107(13):1770-1774. doi:10.1161/01.CIR.0000057811.86187.88

96. Okamoto LE, Shibao CA, Gamboa A, et al. Synergistic pressor effect of atomoxetine and pyridostigmine in patients with neurogenic orthostatic hypotension. *Hypertension*. 2019;73(1):235-241. doi:10.1161/HYPERTENSIONAHA.118.11790

97. Okamoto LE, Shibao C, Gamboa A, et al. Synergistic effect of norepinephrine transporter blockade and α-2 antagonism on blood pressure in autonomic failure. *Hypertension*. 2012;59(3):650-656. doi:10.1161/HYPERTENSIONAHA.111.184812

98. Jarvis SS, Florian JP, Curren MJ, Pawelczyk JA. A somatostatin analog improves tilt table tolerance by decreasing splanchnic vascular conductance. *J Appl Physiol (1985)*. 2012;112(9):1504-1511. doi:10.1152/japplphysiol.01475.2010

99. Armstrong E, Mathias CJ. The effects of the somatostatin analogue, octreotide, on postural hypotension, before and after food ingestion, in primary autonomic failure. *Clin Auton Res*. 1991;1(2):135-140. doi:10.1007/BF01826210

100. Alam M, Smith G, Bleasdale-Barr K, Pavitt DV, Mathias CJ. Effects of the peptide release inhibitor, octreotide, on daytime hypotension and on nocturnal hypertension in primary autonomic failure. *J Hypertens*. 1995;13(12 pt 2):1664-1669.

101. Vloet LC, Mehagnoul-Schipper DJ, Hoefnagels WH, Jansen RW. The influence of low-, normal-, and high-carbohydrate meals on blood pressure in elderly patients with postprandial hypotension. *J Gerontol A Biol Sci Med Sci*. 2001;56(12):M744-M748. doi:10.1093/gerona/56.12.M744

102. Puvi-Rajasingham S, Mathias CJ. Effect of meal size on post-prandial blood pressure and on postural hypotension in primary autonomic failure. *Clin Auton Res*. 1996;6(2):111-114. doi:10.1007/BF02291232

103. Heseltine D, Dakkak M, Woodhouse K, Macdonald IA, Potter JF. The effect of caffeine on postprandial hypotension in the elderly. *J Am Geriatr Soc*. 1991;39(2):160-164. doi:10.1111/j.1532-5415.1991.tb01619.x

104. Furukawa K, Suzuki T, Ishiguro H, et al. Prevention of postprandial hypotension-related syncope by caffeine in a patient with long-standing diabetes mellitus. *Endocr J*. 2020;67(6):585-592. doi:10.1507/endocrj.EJ19-0370

105. Qiao W, Li J, Li Y, et al. Acarbose, the α-glucosidase inhibitor, attenuates the blood pressure and splanchnic blood flow responses to meal in elderly patients with postprandial hypotension concomitant with abnormal glucose metabolism. *Blood Press Monit*. 2016;21(1):38-42. doi:10.1097/MBP.0000000000000160

106. Shibao C, Gamboa A, Diedrich A, et al. Acarbose, an alpha-glucosidase inhibitor, attenuates postprandial hypotension in autonomic failure. *Hypertension*. 2007;50(1):54-61. doi:10.1161/HYPERTENSIONAHA.107.091355

107. Hoeldtke RD, O'Dorisio TM, Boden G. Treatment of autonomic neuropathy with a somatostatin analogue SMS-201-995. *Lancet*. 1986;2(8507):602-605. doi:10.1016/S0140-6736(86)92428-1

108. Raimbach SJ, Cortelli P, Kooner JS, Bannister R, Bloom SR, Mathias CJ. Prevention of glucose-induced hypotension by the somatostatin analogue octreotide (SMS 201-995) in chronic autonomic failure: haemodynamic and hormonal changes. *Clin Sci (Lond)*. 1989;77(6):623-628. doi:10.1042/cs0770623

109. Okamoto LE, Gamboa A, Shibao C, et al. Nocturnal blood pressure dipping in the hypertension of autonomic failure. *Hypertension*. 2009;53(2):363-369. doi:10.1161/HYPERTENSIONAHA.108.124552

110. Park JW, Okamoto LE, Biaggioni I. Advances in the pathophysiology and management of supine hypertension in patients with neurogenic orthostatic hypotension. *Curr Hypertens Rep*. 2022;24(3):45-54. doi:10.1007/s11906-022-01168-7

111. Okamoto LE, Celedonio JE, Smith EC, et al. Continuous positive airway pressure for the treatment of supine hypertension and orthostatic hypotension in autonomic failure. *Hypertension*. 2023;80(3):650-658. doi:10.1161/HYPERTENSIONAHA.122.20081

© 2026 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by guest on 04/07/2026